REMARKS

Claims 64-68 and 70-72 were pending prior to this Response. By the present communication, claims 73-75 have been added, claims 64, 70 and 71 have been canceled and claims 65-68 and 72 have been amended to define Applicants' invention with greater particularity. Support for the claim amendments and newly added claims may be found, among others, at page 12, line 21 to page 13, line 11. Accordingly, claims 65-68 and 70-72 are currently pending in this application.

Applicants thank Examiners Chernyshev and Ulm for the telephonic interview on May 24, 2005.

Claim Objections

Applicants respectfully traverse the objection of claim 64 as allegedly depending from a canceled claim. Applicants have canceled claim 6, rendering the objection moot. Accordingly, withdrawal of the objection is respectfully requested.

Rejection under 35 U.S.C. § 101

Applicants respectfully traverse the rejection of claims 65-68 and 70-72 under 35 U.S.C. § 101 as allegedly being drawn to an invention with no apparent or disclosed specific and substantial credible utility. Applicants have canceled claims 70 and 71, rendering the rejection moot as to those claims.

Specifically, the Examiner alleges that in the absence of the biological significance of these particular claimed nucleic acids, the information that the nucleic acid molecules of SEQ ID NO: 26 or SEQ ID NO: 27 are expressed immediately following seizure does not provide for their specific, substantial and credible utility.

Applicants respectfully submit a declaration under 37 C.F.R. § 1.132 by Dr. Paul Worley (attached herein as Exhibit A) establishing that SEQ ID NO: 26 (clone L-100) is linked to

apoptosis. When neurons in the brain are sufficiently stimulated to produce this protein by a seizure, and the neurons subsequently die, either due to its putative apoptotic action or other cause, the protein would be detectable in the cerebrospinal fluid (CSF). As is known in the art, CSF is easily obtained from a subject by a physician by means of a spinal tap.

Further, the protein sequence of clone L-100 was later shown to be identical to axin 1 up-regulated 1, which has been named Axud1 (see Collins, PNAS, 2002, vol. 99, no. 26, 16899-16903, herein attached as Exhibit B). Axud1 is identical to Mus musculus taip-3 mRNA for TGF-β induced apoptosis protein 3, which has been named taip-3 (see also Salahshor, et al. J. Clin. Pathol. 2005, 58, 225-236, herein attached as Exhibit C). Axin is a multidomain scaffold protein that has many functions in biological signalling pathways. As indicated by Salahshor, the Axin gene is essential for the maintenance of low Wnt signaling activity in the basal state. (Salahshor, page 227, col. 2). "Axin sequence variants have also been found in colon, ovarian, endometrioid, adenocarcinoma and HCC cell lines." (Salahshor, paragraph bridging pages 231 and 232). Finally, Salahshor provides a specific and substantial credible utility for Axin.

> Because axin positively regulates the SAPK/JNK (apoptosis) pathway and negatively regulates the Wnt (survival) pathway, and is the limiting factor in these systems, a search for axin antagonists or agonists might lead to the discovery of compounds that have potential for the treatment of cancer. (Salahshor, page 233, col. 2).

Applicants therefore respectfully submit that the nucleic acid molecules of SEQ ID NO: 26 or SEQ ID NO: 27 have biological significance and thus have specific and substantial credible utility. Accordingly, withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, First Paragraph

Applicants respectfully traverse the rejection of claims 65-68 and 70-72 under 35 U.S.C. § 112, first paragraph as allegedly not being supported by either a clearly asserted utility or a

well established utility. Applicants have canceled claims 70 and 71, rendering the rejection moot as to those claims. For the reasons described above, Applicants respectfully submit that the nucleic acid sequences of SEQ ID NO: 26 or SEQ ID NO: 27 have biological significance and thus have specific and substantial credible utility. Accordingly, withdrawal of the rejection is respectfully requested.

Applicants respectfully traverse the rejection of claims 66-68 and 70-71 under 35 U.S.C. § 112, first paragraph as allegedly failing to comply with the written description requirement. Applicants have canceled claims 70 and 71, rendering the rejection moot as to those claims. The burden of demonstrating that the claims are allegedly not enabled is squarely on the Examiner. *In re Wright*, 999 F.2d 1557, 1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993). The MPEP specifically states that a strong presumption of adequacy of written description exists and directs that § 112, paragraph 1 rejections of an original claim should be rare. MPEP §§ 2163(I)(A) and 2163(II)(A). It is respectfully submitted that in this case the Examiner has not met this burden.

The legal standard for determining the adequacy of written description is clear and well established. The description is adequate if "the disclosure of the application relied upon reasonably conveys to the artisan that the inventor had possession at [the time of filing] of the later claimed subject matter." *Wang Labs Inc. v. Toshiba Corp.*, 993 F.2d 858, 26 USPQ2d 1767. In other words, the question of the lack of adequate written description does not arise unless "one skilled in the art [would not be able] to immediately envisage the product claimed..." *Fujikawa v. Wattanasin*, 93 F.3d 1559, 39 USPQ2d 1895. It is submitted that applying these broad principles to the present application, it can be unequivocally concluded that the written description in this application adequately supports the claims.

Specifically, the Examiner alleges that one of skill in the art would not be able to envision, based on the disclosure, the detailed chemical structure of the encompassed genus of nucleic acids. It remains Applicants' position, however, that as the invention provides both structural and functional characteristics as set forth above, one of skill in the art would have been able to practice the invention

as claimed, at the time of filing of the invention without undue experimentation. It is noted that as amended, claim 66 requires that the claimed isolated nucleic acid not only comprise at least 40 bases in length and hybridize to SEQ ID NO: 26, but also that the nucleic acid sequence is expressed in response to seizure in a subject. Support for this functional aspect is described above, in the declaration under 37 C.F.R. § 1.132 by Dr. Paul Worley, and in Exhibits B and C. As such, the claimed isolated nucleic acid has both structural and functional characteristics. As such, one of skill in the art would have been able to practice the present invention and generate polynucleotide and polypeptide sequences according to the claimed invention. Withdrawal of the rejection is respectfully requested.

Rejection under 35 U.S.C. § 112, Second Paragraph

Applicants respectfully traverse the rejection of claim 64 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically, the Examiner alleges that claim 64 depends from a canceled claim, and therefore, the metes and bounds of the claimed subject matter cannot be determined. Applicants have canceled claim 64, rendering the rejection moot. Withdrawal of the rejection is respectfully requested.

Conclusion

In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application. The Commissioner is hereby authorized to charge any other fees associated with the filing submitted herewith, or credit any overpayments to Deposit Account No. 07-1896.

Respectfully submitted,

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